Contains NO CBI

(1)

RHÔNE-POULENC

TOXICOLOGY DEPARTMENT
P.O. BOX 12014, 2 T.W. ALEXANDER DRIVE
RESEARCH TRIANGLE PARK, NC 27709
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INTERNATIONAL TELEX NUMBER 4999378–ANSWERBACK APC RTP

92 SEP 21 AM 7:57

September 14, 1992

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED
P 713 002 909

8EHQ-92-12600

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Document Processing Center (TS-790)
Office of Toxic Substances
US Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID No.: 8ECAP - 0004

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN 5266, Princeton, NJ 08543-5266) and its subsidiary Rhône-Poulenc Ag Company, the attached study report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program and the Agreement for a TSCA Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA.

The enclosed study report provides information on a 5% granular pesticide formulation of chlormephos. The CAS number assigned to chlormephos is 24934-91-6. The CAS name is S-(chloromethyl) O,O-diethyl phosphorodithioate. This chemical was manufactured in Europe and imported for pesticide research and development. To our knowledge, a pesticide application on this chemical has never been submitted to EPA under the Federal Insecticide, Fungicide, and Rodenticide Act.

No claims of confidentiality are made for this submission. The title of the enclosed report is "Acute Percutaneous Toxicity To Rats Of Chlormephos 5% Granules". The following is a summary of the adverse effects observed in this study.

This study is being submitted under Section 8(e) because of the observation of tremors, ataxia, and salivation. Chlormephos 5% granules was applied as a suspension in corn oil to the shaved backs of rats (10 rats/sex/dose). Doses ranged from 5 to 10 g/kg for males and 2.5 to 5 g/kg for females. Signs of reaction to treatment observed shortly after dosing consisted of lethargy, tremors, ataxia, salivation, and hemorrhaging around the eyes. Death occurred between 19 hours and 7 days after dosing. Recovery of survivors, as judged by external appearance and behavior, occurred within one week after dosing. The dermal LD50 for male rats was 6.3 g/kg with 95% confidence limits of 5.0 to 8.0 g/kg. The dermal LD50 for female rats was 2.6 g/kg with 95% confidence limits of 2.1 to 3.2 g/kg.

DISCLOSURE 3/16/95

One previous TSCA Section 8(e) notice was submitted on this chemical on August 31, 1978. We do not have an EPA Document Control Number for this submission in our records. In addition, approximately 15 submissions will be made on chlormephos under the CAP.

In total, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,

Glenn S. Simon, PhD, DABT
Director of Toxicology

CONFIDENTIAL

1311/D8/72

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ACUTE PERCUTANEOUS TOXICITY TO RATS OF CHLORMEPHOS 5% GRANULES

Addressee:

Dr.A. Thizy,
Pepro,
BP 139 Lyon RP,
69212 Lyon Ceder 1,
FRANCE

1 January, 1973

Authors:

Ronald E. Davies
Jill C. Halliday

Huntingdon Research Centre
Huntingdon,
ENGLAND

HUNTINGDON RESEARCH CENTRE

Division of Toxicology

Sample Designation: Chlormephos, MC2188, 5% granules

Examination for: Acute percutaneous toxicity to rats

Date examined: October-December 1972

EXPERIMENTAL PROCEDURE

The rats used in this investigation were of the CFY strain in the weight range 242 to 372g for males and 202 to 290g for females.

On the day prior to treatment, hair was removed from the dorso-lumbar region of each rat with electric clippers, exposing an area equivalent to 10% of the total body surface. No shaving or chemical depilation was used.

The Chlormephos 5% granules were prepared as a 75% suspension for male rats and 50% suspension for female rats, in corn oil, and were spread evenly over the prepared skin. The treated area was then promptly covered with aluminium foil which was held in place with "Sleek" waterproof plaster encircled firmly round the trunk. Animals similarly treated, using the vehicle alone, served as controls.

At the end of the 24 hours exposure period, the dressings were carefully removed and the treated area of skin decontaminated by washing with warm (40-50°C) dilute soap solution, rinsing in clean warm water and finally blotting dry with absorbent paper.

The decontaminated animals were returned to their cages for a subsequent observation period of 14 days, during which a record was kept of all signs of toxicity.

From the mortality data recorded in Tables 1 and 2, the LD_{50} and its 95% confidence limits were calculated by the method of Weil, C.S. (1952), Biometrics 8, 249 for male rats, and by the method of Litchfield J.T. and Wilcoxon, F. (1949), J. Pharmac. exp. Ther., 96, 99 for female rats.

RESULTS

Groups of rats (ten males or ten females) were treated with Chlormephos 5% granules at varying dosages from 5 to 10g/kg for males, and from 2.5 to 5g/kg for females.

Signs of reaction to treatment, observed shortly after dosing consisted of lethargy, varying degrees of tremoring, ataxia, salivation and haemorrhage around the eyes.

Death occurred between 19 hours and 7 days after dosing. Autopsy revealed congestion of the lungs.

Recovery of survivors, as judged by external appearance and behaviour, was apparently complete within one week. This observation was substantiated by normal bodyweight increases (Tables 1 and 2). Autopsy findings were normal.

CONCLUSION

The acute median lethal percutaneous dosages (LD_{50}'s) and 95% confidence limits to rats of Chlormephos MC2188 5% granules were found to be:

. for male rats 6.3 (5.0 to 8.0)g/kg bodyweight

and for female rats 2.6 (2.1 to 3.2)g/kg bodyweight.

TABLE 1

Mortality ratio and group mean bodyweight (g) of male rats dosed percutaneously with Chlormephos 5% granules

Sex	Dosage (g/kg)	Bodyweight (g) at			Mortality ratio (No. of deaths / No. dosed)	Time of death after dosing (hours)
		Dosing	1 week	2 weeks		
♂	0	294	307	363	0/10	-
	5	285	289	349	2/10	<4 days
	6.4	338	350	402	8/10	<45
	8.0	329	349	387	5/10	<69
	10.0	288	251	319	7/10	<8 days

TABLE 2

Mortality ratio and group mean bodyweight (g) of female rats dosed percutaneously with Chlormephos 5% granules

Sex	Dosage (mg/kg)	Bodyweight (g) at Dosing	Bodyweight (g) at 1 week	Bodyweight (g) at 2 weeks	Mortality ratio (No. of deaths / No. dosed)	Time of death after dosing (hours)
♀	0	247	253	276	0/10	-
	2.5	254	254	274	5/10	<70
	3.2	239	260	278	7/10	<69
	4.0	252	255	274	9/10	<69
	5.0	241	191	died	10/10	<7 days

Triage of 8(e) Submissions

Date sent to triage: 2/5/96 NON-CAP (CAP)

Submission number: 12600A TSCA Inventory: Y N (D)

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN (w/NEUR)

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (0) 1 2 **pages** 1,2 **pages** 1,2,4,5

Notes:

Contractor reviewer : LPS **Date:** 5/11/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 - 12600 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Rhone - Poulenc

Inc.

SUB. DATE: 09/14/92 OTS DATE: 09/21/92 CSRAD DATE: 03/16/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER ENTRY
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:
Chlormephos
Phosphorodithioate, S-(Chloromethyl)
O,O-diethyl

CAS#
24934-91-6
11

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY
YES
CAS SR
NO
IN TERMINI

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
Rat

TOXICOLOGICAL CONCERN:
LOW Acute Dermal Toxicity
MED
HIGH

USE:
R&D
pesticide

PRODUCTION:
import

COMMENTS:

#12600A
L

Acute dermal toxicity is of low concern based on calculated LD_{50}'s of 6300 and 2600 mg/kg in male and female rats, respectively. Mortality and corresponding doses (mg/kg) for males were 2/10 (5000), 8/10 (6400), 5/10 (8000) and 7/10 (10000). Mortality and corresponding doses (mg/kg) for females were 5/10 (2500), 7/10 (3200), 9/10 (4000) and 10/10 (5000). Signs of toxicity included lethargy, tremors, ataxia, salivation and hemorrhage around the eyes (doses not reported).